Current Prevention and Treatment Strategies for Influenza

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FACULTY:

Ruben J. Rucoba, MD
Instructor in Pediatrics,
Northwestern University Feinberg School of Medicine

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Ruben Ruboca has no actual or potential conflict of interest in relation to this program.

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Program Overview:

To provide pharmacists, pharmacy technicians, and nurses with an understanding of current prevention and treatment strategies for influenza.

OBJECTIVES:

After completing this program, pharmacists and nurses will be able to:

- Describe the epidemiology of influenza
- Identify the various pharmaceutical options for the prevention of influenza to include ease of use, comparative efficacy, and contraindications of vaccines.
- Describe the pharmacist’s role in the prevention and treatment of influenza.

Pharmacy Technicians will be able to:

- In general describe the signs and symptoms of the flu.
- Identify the medications used to treat the flu.
Current Prevention and Treatment Strategies for Influenza

by Ruben J. Rucoba, MD
Instructor in Pediatrics,
Northwestern University Feinberg School of Medicine

Esther J. is an 85 year-old Caucasian woman who is a frequent visitor to your retail pharmacy. Her medical problems include hypertension, glaucoma, and COPD. She is currently taking Norvasc, timolol eye drops, and Combivent inhaler. She uses some oxygen at night. Her daughter, Carmen, was in the pharmacy today to pick up her mom’s medication: she was just diagnosed with the flu. Carmen has a few questions for you:

1. Esther has no vomiting and diarrhea—how can she have the flu?
2. Esther got a flu shot two years ago—shouldn’t that have protected her?

Introduction
Influenza is a killer. It’s a common illness, and each winter, everyone knows somebody who comes down with the flu. But most of us overlook its fatal power and catastrophic potential. In the 1918 Spanish Flu pandemic, influenza killed between 50 million to 100 million people worldwide, more than any other disease outbreak in human history (Barry). That was the worst of the occasional pandemics, but new ones occur with persistent regularity, such as the H1N1 pandemic of 2009. Health care providers need to do their part to educate the public, and prevent and treat the flu. Pharmacists are uniquely positioned to assist in this effort.

Clinical Picture
Influenza is a respiratory illness, marked by fever, cough, body aches or myalgia, headaches, fatigue, sore throat, and runny or stuffy nose. Sometimes, patients complain of dizziness, vomiting and upset stomach, especially children (Centers for Disease Control and Prevention "Flu Symptoms & Severity"). But bear in mind that many lay-people think “the flu” is synonymous with gastroenteritis, a viral infection causing vomiting and diarrhea. Though this is commonly referred to as the “stomach flu,” it is a completely different disease from influenza. This explains Carmen’s confusion about her mother having the “flu” despite a lack of GI symptoms. When speaking to the lay-public, all health care providers should remember to use “the flu” for true influenza, and some other phrase (“stomach virus,” or “a stomach bug”) for gastroenteritis.

Though most people who get the flu recover completely, some will develop complications, a few of which can be fatal. Common complications include pneumonia, bronchitis, and sinus and ear infections. The flu can worsen underlying health conditions, including asthma and congestive heart disease (Centers for Disease Control and Prevention "Flu Symptoms & Severity").

Epidemiology
Experts have a difficult time arriving at the exact number of influenza cases each year, as many people who have the flu do not seek medical attention. However, hospitalization rates are
closely monitored by the Centers for Disease Control and Prevention (CDC). For the last year for which data is available, 2009-2010, the rate of hospitalization for influenza was highest in those under 4 years, at 8.3 hospitalizations per 10,000. Every other age group, including those over 65 years, had a hospitalization rate between 3.2 and 3.8 per 10,000 (Centers for Disease Control and Prevention "Update: Influenza Activity - United States, 2009-10 Season"). That year included the H1N1 pandemic, so hospitalization rates were higher than normal across all age groups.

The CDC also tracks deaths from influenza. Some years are worse than others. The CDC compiled data from 1976-2007 to get a better idea of how many deaths are caused by the flu over a relatively long time period. The annual number of deaths associated with seasonal influenza during that time ranged from as low as 3,349 in 1986-1987 to as high as 48,614 in 2003-2004. Over those 31 years, the flu killed an average of 23,607 people annually. Of these deaths, 87.9% were in persons aged ≥ 65 years (Centers for Disease Control and Prevention "Estimates of Deaths Associated with Seasonal Influenza --- United States, 1976-2007").

But it’s not just the young and the old who are at high risk—anyone with a chronic illness is susceptible to complications from the flu. The highest risk groups include those with asthma or chronic lung disease (like your patient Esther, who has COPD), neurological and neurodevelopmental conditions, heart disease, blood disorders, endocrine diseases such as diabetes, kidney and liver disease, metabolic disorders, the morbidly obese and pregnant women (Centers for Disease Control and Prevention "People at High Risk of Developing Flu-Related Complications").

The data above demonstrate a key characteristic of influenza: the highest risk groups are the very young, the very old, and those with underlying medical conditions at any age. These are the most vulnerable populations, and every effort should be made to protect these groups with a flu vaccine every year.

But why do we need to get a flu shot every year? Most other vaccines are given just a few times, and last for life. What makes influenza different? The answer is found in the basic science of virology.

**Basic Science**

Influenza is a virus, and it can change in two ways. The first is known as “antigenic drift,” in which the virus changes its antigens just a little bit every year. Antigens are the proteins on microbes that are recognized by our circulating antibodies to help destroy and eliminate the germ. This antigenic drift causes the body’s immune system not to recognize the “new” virus, so a person’s antibodies against the flu virus are less effective, or not effective at all (Fiore, Uyeki, et al.). This annual change is the main reason that we need a flu shot every year, which answers Carmen’s question about why her mother’s flu shot from two years ago didn’t protect her.

The second change is “antigenic shift,” which occurs much less frequently. Antigenic shift is a major change in the proteins of the virus, so that most people have little or no protection against this novel strain. Antigenic shift is responsible for the periodic pandemics. This is what
occurred in spring 2009 when the H1N1 spread quickly because few people were immune to it (Fiore, Uyeki, et al.).

**Prevention**

Because influenza treatment is only partially effective, prevention is paramount, and the mainstay of prevention is the influenza vaccine. There are essentially two types of vaccine: trivalent inactivated influenza vaccine (TIV) and live, attenuated influenza vaccine (LAIV). The TIV is inactivated or killed, so it cannot give the recipient the flu. It is administered as a shot. The LAIV, however, is a live virus that has a theoretical risk of transmitting the flu to the recipient or close contacts of the recipient. It is administered as a nasal spray. Both types contain identical viruses: the annual flu vaccine consists of two types of Influenza A and one type of influenza B. The strains used are related to the strains from previous years (Fiore, Uyeki, et al.).

The table below summarizes the major differences and similarities between the two vaccines (Fiore, Uyeki, et al.):

**Table 1. Trivalent inactivated influenza vaccine (TIV) compared with live, attenuated influenza vaccine (LAIV) for seasonal influenza, US formulations**

<table>
<thead>
<tr>
<th>Factor</th>
<th>TIV</th>
<th>LAIV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Route of administration</td>
<td>Intramuscular injection</td>
<td>Intranasal spray</td>
</tr>
<tr>
<td>Type of vaccine</td>
<td>Killed virus</td>
<td>Live virus</td>
</tr>
<tr>
<td>Number of included virus strains</td>
<td>3 (2 influenza A, 1 influenza B)</td>
<td>3 (2 influenza A, 1 influenza B)</td>
</tr>
<tr>
<td>Vaccine virus strains updated</td>
<td>Annually</td>
<td>Annually</td>
</tr>
<tr>
<td>Frequency of administration</td>
<td>Annually*</td>
<td>Annually*</td>
</tr>
<tr>
<td>Approved age</td>
<td>≥ 6 months^</td>
<td>2-49 yrs+</td>
</tr>
<tr>
<td>Interval between 2 doses for children ≥ 6 mos-8 yrs who are receiving flu vaccine for the first time</td>
<td>≥ 4 weeks</td>
<td>≥ 4 weeks</td>
</tr>
<tr>
<td>Can be given to persons with medical risk factors for influenza-related complications+</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Can be given to children with asthma or children aged 2-4 yrs with wheezing the past year^x</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Can be administered to family member/close contacts of immunosuppressed persons not requiring a protected environment</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Can be administered to family member/close contacts of immunosuppressed persons requiring a protected environment (e.g., stem cell transplant recipient)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Can be administered simultaneously with other vaccines</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>If not administered simultaneously, can be administered within 4 weeks of another live vaccine</td>
<td>Yes</td>
<td>Prudent to space 2-4 wks apart</td>
</tr>
<tr>
<td>If not administered simultaneously, can be administered within 4 weeks of an inactivated vaccine</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Children aged 6 months-8 years who have never received a seasonal influenza vaccine before or who did not receive at least 1 dose of influenza A (H1N1) 2009 monovalent vaccine should receive 2 doses, spaced ≥ 4 weeks apart. Those children aged 6 months-8 years who were vaccinated for the first time in the 2009-10 season with the seasonal 2009-10 vaccine but who received only 1 dose of the seasonal influenza vaccine should receive 2 doses in the following year, spaced ≥ 4 weeks apart.

Approval varies by formulation. Fluzone (sanofi pasteur) has been approved previously for use in children as young as age 6 months. Fluzone High-Dose is approved for use in persons aged > 65 years. Immunization providers should check FDA-approved prescribing information for influenza vaccines for the most updated information.

Persons at higher risk for complications of influenza infection because of underlying conditions should not receive LAIV. Such persons include those who have chronic pulmonary (including asthma), cardiovascular (except hypertension), renal, hepatic, neurologic, hematologic, or metabolic (including diabetes mellitus) disorders; those who are immunosuppressed (including immunosuppression caused by medications or by HIV); those who are or will be pregnant during the flu season; those aged 6 months -18 years and receiving long-term aspirin therapy and who therefore might be at risk for experiencing Reye syndrome after influenza virus infection; and residents of nursing homes and other chronic-care facilities.

Clinicians and vaccination programs should screen for possible reactive airways diseases when considering use of LAIV for children aged 2-4 years and should avoid use of this vaccine in children with asthma or a recent wheezing episode. Health-care providers should consult the medical record, when available, to identify children aged 2-4 years with asthma or recurrent wheezing that might indicate asthma. In addition, to identify children who might be at greater risk of asthma and possibly at increased risk for wheezing after receiving LAIV, parents of caregivers for children aged 2-4 years should be asked: “In the past 12 months, has a health-care provider ever told you that your child had wheezing or asthma?” Children whose parents answer “yes” to this question and children who have asthma or who had a wheezing episode noted in the medical record within the preceding 12 months should not receive LAIV.

Studies have demonstrated reduced efficacy of influenza vaccination in the elderly (> 65 years), the exact population who is most at risk for death from influenza (Dorrell et al.; McElhaney et al.). For this reason, a new type of TIV has been produced, called Fluzone High-Dose, which has an increased amount of influenza antigen compared with other TIV vaccines (180 mcg vs 45 mcg of hemagglutinin of flu antigen per dose) (Food and Drug Administration). Several studies have shown higher antibody response to this new high-dose vaccine, but it is unclear if this will ultimately lead to greater protection from influenza infection and its complications (Couch et al.; Falsey et al.; Keitel et al.)

Another new product that is approved for the 2011-12 flu season is Fluzone Intradermal. The premise of this version is that the skin has some specialized cells called dendritic cells that play a role in our immune response. Because it is intradermal, the volume of the shot is much smaller, as is the antigenic dose: 0.1 ml containing only 27 mcg hemagglutinin. The initial studies suggest it is just as efficacious as the usual intramuscular shot, but has a higher incidence of local adverse effects, such as redness, swelling and itching at the injection site (Food and Drug Administration).

In fact, though there are really only two classes of vaccine, there are many formulations on the market. Table 2 summarizes the current FDA-approved vaccines for the 2010-11 season.
<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Trade Name</th>
<th>Manufacturer</th>
<th>Presentation</th>
<th>Mercury content (mcg/0.5 ml dose)</th>
<th>Age group</th>
<th>No. of doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIV</td>
<td>Fluzone</td>
<td>sanofi pasteur</td>
<td>0.25 ml prefilled syringe</td>
<td>0.0</td>
<td>6–35 mos</td>
<td>1 or 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.5 ml prefilled syringe</td>
<td>0.0</td>
<td>≥ 36 mos</td>
<td>1 or 2*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.5 ml vial</td>
<td>0.0</td>
<td>≥ 36 mos</td>
<td>1 or 2*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5.0 ml multidose vial</td>
<td>25.0</td>
<td>≥ 6 mos</td>
<td>1 or 2*</td>
</tr>
<tr>
<td>TIV</td>
<td>Fluvirin</td>
<td>Novartis Vaccine</td>
<td>5.0 ml multidose vial</td>
<td>24.5</td>
<td>≥ 4 yrs</td>
<td>1 or 2*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.5 ml prefilled syringe</td>
<td>&lt; 1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TIV</td>
<td>Fluarix</td>
<td>Glaxo SmithKline</td>
<td>0.5 ml prefilled syringe</td>
<td>0.0</td>
<td>≥ 3 yrs</td>
<td>1</td>
</tr>
<tr>
<td>TIV</td>
<td>FluLaval</td>
<td>Glaxo SmithKline</td>
<td>5.0 ml multidose vial</td>
<td>25.0</td>
<td>≥ 18 yrs</td>
<td>1</td>
</tr>
<tr>
<td>TIV</td>
<td>AFLuria</td>
<td>CSL Biotherapies</td>
<td>0.5 ml prefilled syringe</td>
<td>0.0</td>
<td>≥ 9 yrs^</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5.0 ml multidose vial</td>
<td>25.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TIV</td>
<td>Fluzone High-Dose</td>
<td>sanofi pasteur</td>
<td>0.5 ml prefilled syringe</td>
<td>0.0</td>
<td>≥ 65 yrs</td>
<td>1</td>
</tr>
<tr>
<td>TIV</td>
<td>Fluzone Intradermal</td>
<td>sanofi pasteur</td>
<td>0.1 ml prefilled syringe</td>
<td>0.0</td>
<td>18-64 yrs</td>
<td>1</td>
</tr>
<tr>
<td>LAIV</td>
<td>FluMist X</td>
<td>MedImmune</td>
<td>0.2 ml sprayer, divided dose</td>
<td>0.0</td>
<td>2-49 yrs</td>
<td>1 or 2*</td>
</tr>
</tbody>
</table>

*Children aged 6 months-8 years who have never received a seasonal influenza vaccine before or who did not receive at least 1 dose of influenza A (H1N1) 2009 monovalent vaccine should receive 2 doses, spaced ≥ 4 weeks apart. Those children aged 6 months-8 years who were vaccinated for the first time in the 2009-10 season with the seasonal 2009-10 vaccine but who received only 1 dose of the seasonal influenza vaccine should receive 2 doses in the following year, spaced ≥ 4 weeks apart.

^Because of the increased frequency of fevers and febrile seizures in children aged 6 months through 4 years and increased frequency of fevers in children aged 5-8 years, the ACIP recommends not using Afluria in children aged 6 months through 8 years (Centers for Disease Control and Prevention "Update: Recommendations of the Advisory Committee on Immunization Practices (Acip) Regarding Use of Csl Seasonal Influenza Vaccine (Afluria) in the United States During 2010-11").
Fluzone intradermal is licensed for use in the 2011-12 flu season, and is given as in intradermal injection.

All TIV doses are given intramuscularly, except for Fluzone Intradermal. For adults and older children, the recommended site of vaccination is the deltoid muscle. The preferred site for infants and young children is the anterolateral aspect of the thigh.

Flumist is shipped refrigerated and stored in the refrigerator at 36°F-46°F (2°C-8°C) after arrival in the vaccination clinic. The dose is 0.2 ml divided equally between each nostril.

Based on the above information, Esther J. would benefit from either a regular TIV dose of vaccine or the Fluzone High-Dose vaccine next year.

Despite the formal recommendation from the CDC’s Advisory Committee on Immunization Practices (ACIP) in 2010 that all persons older than 6 months of age get a flu vaccine, vaccine uptake is still woefully short of national goals. For the 2008-09 season, uptake ranged from 11.3% of pregnant women to 65.5% of those ≥ 65 years old (Fiore, Uyeki, et al.). But this is where pharmacists have a crucial role to play. One study demonstrated the benefit of community pharmacists offering flu vaccine throughout the season as opposed to a single day (Grabenstein). Community based pharmacists should bring up the flu shot every time a patient comes for a prescription, especially in those at highest risk. Advocating for and administering the flu vaccine has been called a “duty” of health care workers (Grabenstein and Bonasso).

And hospital pharmacists play a key role in advocating for standing-order vaccination programs for inpatients (Sokos; Ovbiagele et al.) But again, the numbers show that there is much work to be done. A recent study showed that in one flu season, of 23,404 Medicare recipients hospitalized for a non-influenza illness, 97.3% of them were not vaccinated against influenza before discharge (Bratzler et al.) Hospital-based pharmacists can be effective advocates in reminding the clinical care team of the importance of pre-discharge flu vaccinations.

Although influenza vaccination is the key to prevention, there are people who should not receive a flu vaccine without first consulting a physician. These include people who have a severe allergy to chicken eggs (the vaccine is grown in eggs), people who have had a severe reaction to an influenza vaccination, people who developed Guillain-Barre syndrome within six weeks of getting an influenza vaccine, children less than 6 months old, and people who have a moderate-to-severe illness with a fever (they should wait until they recover to get vaccinated) (Centers for Disease Control and Prevention "Key Facts About Seasonal Flu Vaccine").

Pharmacists who administer flu vaccine should advise their patients that some side effects may occur after vaccination. The TIV shot can result in soreness, redness or swelling at the site of injection, low grade fever, and muscle aches. The LAIV spray may result in some flu like symptoms, including wheezing, runny nose, headache, vomiting, muscle aches, fever, sore throat and cough (Centers for Disease Control and Prevention "Key Facts About Seasonal Flu Vaccine").

Although the vaccine is the most important component of prevention, it isn’t the only one. A Cochrane review of hundreds of studies showed that simple measures like handwashing, isolation of influenza patients in the hospital, and barriers to transmission (gloves, gowns, masks) can be effective in reducing the spread of influenza (Jefferson, Del Mar, et al.) Washing your
hands frequently during flu season will help prevent the spread of flu, and is a good example to set for your employees or co-workers.

But even with all that prevention, people still get the flu. Fortunately, over the last few years, newer antiviral medications can help treat the flu.

**Treatment**

*While discussing Esther’s condition with her daughter, Carmen, you ask how the rest of the family is doing. She notes that her 4 year-old twins who have asthma have been doing really well lately, and haven’t used their albuterol inhalers in a long time. She also mentions that her 9 month-old is doing well. You know that Esther lives with Carmen and her family. Carmen has a few more questions for you:*

1. Will her mom’s medicine, Tamiflu, interfere with any of her other medicines?
2. Will the Tamiflu cause any side effects?
3. What can she do to keep the others in the house from getting the flu?

There are currently four licensed antiviral medications available to treat influenza in the US: amantadine (Symadine, Symmetrel), rimantadine (Flumadine), zanamivir (Relenza), and oseltamivir (Tamiflu). However, amantadine and rimantadine, classified as adamantanes, are not active against influenza B strains, and up to 96% of the influenza A strains are resistant to these drugs. Therefore, both amantadine and rimantadine are not recommended for treatment or prevention of influenza in the US (Fiore, Fry, et al.)

Zanamivir and oseltamivir are neuraminidase inhibitors, and nearly all strains of influenza A and B are sensitive to these medicines (Fiore, Fry, et al.). When used for treatment, these antivirals can reduce the severity and duration of symptoms, but they need to be started early in the course of illness to be effective. The ACIP’s official recommendation is that these medicines should be started within 48 hours of the start of symptoms. Several studies showed that the use of neuraminidase inhibitors reduce the duration of symptoms by about 1-2 days (Hayden et al.; Monto et al.; Jefferson, Demicheli, et al.). A recent Cochrane review of 51 randomized controlled trials found that zanamivir and oseltamivir are between 61% and 73% efficacious against symptomatic influenza (Jefferson, Demicheli, et al.)

These medicines are also effective at preventing some of the serious complications of the flu. One meta-analysis showed a significant reduction in pneumonia and hospitalizations in influenza patients receiving oseltamivir (Kaiser et al.)

These medicines are indicated not only for treatment, but for prevention as well. In those who are high risk for developing complications from the flu and have been exposed to influenza but are currently asymptomatic, the neuraminidase inhibitors can be given at lower doses as chemoprophylaxis against influenza. Otherwise healthy people can also receive chemoprophylaxis if desired. The table below summarizes the use of these two medicines (Fiore, Fry, et al.)
Table 3. Recommended dosage and schedule of influenza antiviral medications* for treatment^ and chemoprophylaxis%.  

<table>
<thead>
<tr>
<th>Antiviral agent</th>
<th>Age group (yrs)</th>
<th>1-6</th>
<th>7-9</th>
<th>10-12</th>
<th>13-64</th>
<th>≥ 65</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zanamivir</td>
<td>Treatment, influenza A &amp; B</td>
<td>Not approved</td>
<td>10 mg (2 inhalations) twice daily</td>
<td>10 mg (2 inhalations) twice daily</td>
<td>10 mg (2 inhalations) twice daily</td>
<td>10 mg (2 inhalations) twice daily</td>
</tr>
<tr>
<td></td>
<td>Chemoprophylaxis, influenza A &amp; B</td>
<td>Not approved for ages 1-4</td>
<td>Ages 5-9</td>
<td>10 mg (2 inhalations) twice daily</td>
<td>10 mg (2 inhalations) twice daily</td>
<td>10 mg (2 inhalations) twice daily</td>
</tr>
<tr>
<td>Oseltamivir#</td>
<td>Treatment,** influenza A &amp;B</td>
<td>Dose varies by child’s weight</td>
<td>Dose varies by child’s weight</td>
<td>Dose varies by child’s weight &gt;40 kg = adult dose</td>
<td>75 mg twice daily</td>
<td>75 mg twice daily</td>
</tr>
<tr>
<td></td>
<td>Chemoprophylaxis, influenza A &amp; B</td>
<td>Dose varies by child’s weight</td>
<td>Dose varies by child’s weight</td>
<td>Dose varies by child’s weight &gt;40 kg = adult dose</td>
<td>75 mg once daily</td>
<td>75 mg once daily</td>
</tr>
</tbody>
</table>

*Zanamivir is manufactured by GlaxoSmithKline (Relenza—inhaled powder). Zanamivir is approved for treatment of persons aged ≥7 years and approved for chemoprophylaxis of persons aged ≥5 years. Zanamivir is administered through oral inhalation by using a plastic device included in the medication package. Patients will benefit from instruction and demonstration of the correct use of the device. Zanamivir is not recommended for those persons with underlying airway disease. Oseltamivir is manufactured by Roche Pharmaceuticals (Tamiflu-tablet). Oseltamivir is approved for treatment or chemoprophylaxis of persons aged ≥1 year. Oseltamivir is available for oral administration in 30 mg, 45 mg, and 75 mg capsules and liquid suspension. No antiviral medications are approved for treatment or chemoprophylaxis of influenza among children aged <1 year. This information is based on data published by the Food and Drug Administration (FDA), available at [http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm100228.htm](http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm100228.htm).

^Recommended duration for antiviral treatment is 5 days. Longer treatment courses can be considered for patients who remain severely ill after 5 days of treatment.

%Recommended duration is 10 days when administered after a household exposure and 7 days after the most recent known exposure in other situations. For control of outbreaks in long-term care facilities and hospitals, CDC recommends antiviral chemoprophylaxis for a minimum of 2 weeks and up to 1 week after the most recent known case was identified.

#See below for discussion on use of oseltamivir for infants < 1 year. A reduction in the dose of oseltamivir is recommended for persons with creatinine clearance < 30mL/min.

**Treatment with oseltamivir for children aged ≥ 1 year who weight ≤ 15 kg is 30 mg twice a day. For children who weigh 15-23 kg, the dose is 45 mg twice a day. For children who weight 23-40 kg, the dose is 60 mg twice a day. For children who weigh > 40 kg, the dose is 75 mg once a day. The chemoprophylaxis dose is the same as the treatment dose, but given only once daily. For children, oseltamivir comes as a suspension or can be compounded into a suspension.
Oseltamivir currently is not approved by the FDA for use in children less than 1 year old, but the CDC recommends the dosing schedule listed below in Table 4 to treat and chemoprophylaxis children aged 3-11 months (Fiore, Fry, et al.)

Table 4. Dosing recommendations for treatment or chemoprophylaxis of children aged < 1 year using oseltamivir

<table>
<thead>
<tr>
<th>Age</th>
<th>Recommended treatment dose for 5 days</th>
<th>Recommended chemoprophylaxis dose for 10 days*</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 3 mos</td>
<td>3 mg/kg/dose twice daily</td>
<td>Not recommended unless situation judged critical because of limited data on use in this age group</td>
</tr>
<tr>
<td>3-11 mos</td>
<td>3 mg/kg/dose twice daily</td>
<td>3 mg/kg/dose once daily</td>
</tr>
</tbody>
</table>

*Current weight-based dosing recommendations are not appropriate for premature infants. Premature infants might have slower clearance of oseltamivir because of immature renal function, and doses recommended for full-term infants might lead to very high drug concentrations in this age group. Very limited data from a small cohort of premature infants suggested that oseltamivir concentrations among premature infants administered oseltamivir 1 mg/kg twice daily would be similar to those observed with the recommended treatment dose in term infants (3 mg/kg twice daily). Observed drug concentrations were highly variable among premature infants. These data are insufficient to recommend a specific dose of oseltamivir for premature infants.

Side effects of zanamivir include diarrhea, nausea, sinusitis, bronchitis, cough, headache dizziness and ear, nose and throat infections. But all of these effects were noted in less than 5% of patients. Zanamivir is given as an inhalation, and is not approved for persons with underlying respiratory disease. Side effects of oseltamivir include nausea and vomiting in 6% to 14% of patients, but these effects are decreased if the medicine is taken with food (Fiore, Fry, et al.)

Interactions between these medicines and other drugs are rare. Pharmacokinetic studies have suggested that there are no significant drug interactions with either zanamivir (Daniel, Barnett and Pearson) or oseltamivir (Hill et al.)

Pregnancy is not a contraindication to use of the neuraminidase inhibitors. Both drugs are classified as Pregnancy Category C medications, meaning there is not enough data to assess the safety of these drugs in pregnant women. Of the two, oseltamivir is the preferred medicine (Fiore, Fry, et al.)

In time, resistance against zanamivir and oseltamivir will assuredly develop, but newer antivirals are being tested against influenza (Boltz et al.) Pharmacists need to keep abreast of the latest information regarding drug resistance in their community. This information can be found in the CDC’s Morbidity and Mortality Weekly Report at www.cdc.gov/mmwr. Other useful influenza information can be found there as well, including influenza surveillance and updates on adverse effects of newer flu vaccines and treatments.

You can now confidently answer Carmen’s questions. You can reassure her that Tamiflu is the best choice of medicine to fight her influenza, and that Esther can safely take the Tamiflu with her other medications. Reassure her that the only side effects are nausea and vomiting, which may be ameliorated by taking the Tamiflu with food. And because all her kids fall into the high-risk category, she should ask their doctor about chemoprophylaxis with Tamiflu.
Conclusion
Influenza is a serious illness, causing significant morbidity and mortality each year. Pharmacists are well-positioned to educate about the flu, provide flu vaccinations in retail pharmacies, establish a standing order set or other systems to ensure hospitalized patients receive a flu shot, and provide counseling on the medicines used to treat the flu.
Bibliography


Centers for Disease Control and Prevention. "People at High Risk of Developing Flu-Related Complications."


